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| 30313 | 7590 | 08/18/2006 | EXAMINER KOLKER, DANIEL E | |
| KNOBBE, MARTENS, OLSON & BEAR, LLP 2040 MAIN STREET IRVINE, CA 92614 | | | ART UNIT 1649 | |

DATE MAILED: 08/18/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/036,063

Applicant(s)

GODDARD ET AL.

Examiner

Daniel Kolker

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 01 May 2006.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 22-26 and 28-30 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 22-26 and 28-30 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date 5/1/06
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____

DETAILED ACTION

1. Applicant's remarks filed 1 May 2006 have been entered. Claims 22 – 26 and 28 – 30 are pending and under examination.
2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Withdrawn Rejections and Objections

3. The following rejections and objections made in the previous office action are withdrawn:

A. The rejection of claims 22 – 26 and 28 – 30 under 35 USC § 101 for lack of utility and the corresponding rejection under 35 USC § 112, first paragraph for lack of enablement is withdrawn. The assay described in Assay 92 (Example 41) uses cultured mouse mesangial cells and determines whether the test protein increases proliferation of the cells *in vitro*. The specification asserts that the claimed proteins are useful in treatment of kidney diseases wherein mesangial cells are damaged. This utility was recognized in the prior art. Hugo (1997. J Clin Invest 100:786-794) teaches that mesangial cells are lost in disease states and that replenishing these cells is useful (see abstract and first paragraph, for example). Proliferation of mesangial cells appears to be required for successful repair of glomeruli following renal injury (Hugo, p. 233). Thus it appears that proliferation of the cells is desirable. This is supported by other articles, also published prior to the effective filing date. For example Savill (1999. Kidney International 56:1216-1222) teaches that while over-proliferation of mesangial cells can be problematic, proliferation is useful for recovery from kidney injury (see pages 1216 – 1217 of Savill). Additionally Schlocklmann (1999. Kidney International 56:1199-1207, of record) teaches that proliferation of mesangial cells is required for successful renal repair (see paragraph spanning 1199 – 1200).

Assay 92 uses a 15% increase in proliferation as a cutoff. While the examiner was unable to find scientific support for this value in the prior art, the post-filing publication by Rovin et al. (2002. Kidney International 61:1293-1302, of record) shows that the threshold is reasonable. An 18% increase in proliferation, measured in a manner essentially identical to that in the application, is statistically significant. See Rovin, paragraph spanning pp. 1295 – 1296. Thus the cutoff point in the assay appears to be reasonable. The assay identifies products which proliferate mesangial cells *in vitro*, and it was well-known in the prior art that such

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proliferation is useful for recovery from diseases. This is in fact what applicant asserted on p. 168 of the specification.

B. The objection to the oath is withdrawn. Applicant argues that since inventors Eaton and Zhang have been deleted as inventors, the objection is moot. Applicant's arguments are persuasive.

Maintained Rejections and Objections

Claim Rejections - 35 USC § 102

4. Claims 22 – 25 and 28 – 29 are rejected under 35 U.S.C. 102(a) as being anticipated by Ruben (WO 99/58660).

This rejection is maintained for the reasons of record. As a preliminary matter, the examiner notes that in the previous office action, this rejection was set forth as two separate rejections over the same reference. On p. 7, paragraph 9, claims 22 – 25 and 28 – 29 were rejected under 35 USC 102(a) over Ruben, and on p. 9, paragraph 11, claims 25 and 28 – 29 were rejected under 35 USC 102(a) over the same reference by Ruben. For the sake of simplicity and clarity, the rejections that had been listed separately are now listed as one rejection. This is believed not to constitute a new grounds of rejection, as all claims included within this rejection had previously been rejected over Ruben (WO 99/58660).

Applicant argues that the declaration filed 20 June 2005, combined with the provisional application (60/130359), filed 21 April 1999, is sufficient to demonstrate conception of the invention prior to the effective date of the reference coupled with due diligence to constructive reduction to practice. Applicant's arguments have been fully considered but they are not persuasive.

To briefly recapitulate the facts of the case: Ruben teaches a protein sequence that is 99.6% identical to the protein of applicant's SEQ ID NO:57. Ruben also teaches antibodies to the sequence, and meets the limitation of claims 22 – 25 and 28 – 29. Applicant is directed to the previous office actions for a more detailed explanation of how the reference by Ruben meets every claim limitation. Applicant did not traverse the examiner's conclusion that the antibodies taught by Ruben are within the scope of claims 22 – 25 and 28 – 29, but rather argues that the declaration and provisional application are evidence of conception and constructive reduction to practice.

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The declaration filed 20 June 2005 provides evidence that applicant was in possession of the protein of SEQ ID NO:57 and in fact knew how to use the protein, as the evidence supplied with the declaration indicates that the protein came up as positive in Assay 92. While no date is provided, the declaration states that the assay was performed and results obtained prior to 18 November 1999, the effective date of the reference by Ruben. As stated previously, the examiner is convinced applicant actually reduced to practice the protein of SEQ ID NO:57 before the date the reference by Ruben was published.

The instant invention, however, is not a protein but is an antibody. Applicant argues that the provisional application filed 21 April 1999 constitutes a constructive reduction to practice. The examiner disagrees. In order for a patent application, including a provisional application, to constitute a constructive reduction to practice, it must conform to 35 USC § 112, first paragraph. That is, it must teach the public how to both make and use the invention, as well as conform to the written description and best mode requirements of the statute. See MPEP § 2138.05, particular subsection I, which refers to the decision *Kawai v. Metlesics*, 480 F.2d 880, 886, 178 USPQ 158, 163 (CCPA 1973), where the court ruled that a constructive reduction to practice is not proven unless the specification discloses a practical utility where one would not be obvious. The examiner does not question whether the best mode and written description criteria are met for the case of monoclonal antibodies, nor is there any doubt that the provisional application teaches how to make the monoclonal antibodies. See, for example, 60/130359, p. 44, which describes monoclonal antibodies, and claims 29 – 31 of the provisional application, which claim antibodies generically, as well as monoclonal and humanized antibodies. However, 60/130359 does not disclose the results of the mesangial cell proliferation assay which are later disclosed in the non-provisional application. The fact that the provisional application does not disclose these results was first made of record in the office action mailed 17 March 2005 (see p. 2 of that office action), and applicant did not traverse the examiner's determination that the first time those results were disclosed was 1 March 2000, the date that PCT/US00/05601 was filed. Thus, the provisional application does not teach how to use the protein, nor does it teach how to use the antibodies now claimed.

Additionally, the provisional application does not provide adequate written description support for the full scope of the inventions now claimed. The examiner is unable to find support for labeled antibodies, which are the subject matter of instant claims 26, or for fragments of antibodies generically (see instant claim 25), or for the specific fragments of the antibodies that

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are set forth in instant claims 28 – 29. Thus the provisional application does not constitute a constructive reduction to practice of the invention of claims 25 – 26 or 28 – 29.

Finally, the declaration does not provide evidence of diligence of the time period between when the experiments were performed and when the provisional application was filed. The entire period must be accounted for; see MPEP 2138.06. In the instant situation, the dates the actual experiment was performed have not been supplied, so the examiner cannot even determine what the duration of that period was. Furthermore, even if the dates had been supplied, there are no statements or other evidence as to how the diligence requirement has been met.

The rejection could be overcome by providing evidence that applicant was in possession of the invention before the effective date of the reference. However in order to do so, the declaration must teach at least as much as the reference. Ruben teaches antibodies to the sequence that is over 99% identical to SEQ ID NO:57. See Ruben, p. 49 lines 8 – 10 which teaches antibodies, as well as p. 49 lines 17 – 20 which teach the specific epitopes to use in making the antibodies. See also Ruben p. 195 line 32 – p. 197 line 3, for a more detailed description of antibodies. Clearly Ruben teaches the invention now claimed. In contrast, the declaration does not teach applicant was in possession of the invention. As it does not teach as much as the reference, it cannot overcome the rejection.

For the reasons above, the declaration and provisional application, taken together, are not sufficient to overcome the rejection under 35 USC § 102(a) over Ruben.

5. Claims 22 – 25 and 28 – 29 are rejected under 35 U.S.C. 102(e) as being anticipated by Ruben (US Patent Application Publication 2003/0100051). For the sake of clarity, this reference is referred to as Ruben II.

This rejection is maintained for the reasons of record. Applicant argues, at the bottom of p. 8 of the remarks, that the effective filing date of the Ruben II is 10 November 1999. Applicant's arguments with respect to the effective filing date are persuasive. As Ruben II claims benefit of an international application which was filed before November 29, 2000, that application cannot be relied upon under 35 USC 102(e). Therefore the examiner agrees that the earliest effective filing date of Ruben II, for the purposes of applying prior art, is 10 November 1999.

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Even though the examiner agrees that the effective filing date of Ruben II is 10 November 1999, applicant's arguments that a declaration filed under 37 CFR § 1.131, combined with the provisional application, are sufficient to antedate the Ruben II reference are not persuasive. First, the remarks filed 1 May 2006 (p. 9, first paragraph) refer to a second declaration by Goddard et al. as "attached herewith". No second declaration has been submitted in this case. Applicant indicates that the declaration was also submitted in Application 10/036342. While the declaration in the other case has not been made of record in the instant case, even if it had been made of record it would not be sufficient to overcome the rejection over Ruben II.

This situation is very similar to the Ruben situation discussed in the rejection under 35 USC 102(a). The difference appears to be in the date to be overcome; the examiner cannot determine any other facts that differ between the two cases. Even if the declaration referred to had been filed, it would not be sufficient to overcome the rejection. Applicant argues, on p. 10 of the remarks, that the invention now claimed had been constructively reduced to practice before the effective date of Ruben II.

Applicant's arguments have been fully considered but they are not persuasive. In the interest of brevity, the reasons why the declarations of record and the provisional application are not sufficient to overcome the rejection will not be repeated. Rather, applicant is referred to the discussion of Ruben (WO 99/58660) above. The declaration referred to in the remarks does not provide evidence of possession or conception of the antibody now claimed, and the provisional application does not teach how to use the antibodies, as it does not disclose the results of the kidney mesangial cell proliferation assay. As the provisional application does not teach how to use the invention now claimed, it is not a constructive reduction to practice. Therefore the declaration from case 10/036342, even if it had been filed in the instant case, would not be sufficient to overcome the rejection.

Furthermore, as described in detail above, the declaration does not teach as much as the reference. The reference teaches antibodies. The declaration does not. Therefore the declaration is not sufficient to overcome the rejection over Ruben II.

Claim Rejections - 35 USC § 103

6. Claims 22 – 26 and 28 – 30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ruben (WO 99/58660) in view of Holmes (Current Protocols in Immunology, cited in previous office action).

As a preliminary matter, claims 23 – 24 and 28 – 29 are included in this rejection. While they were not explicitly listed in the grounds of rejection in the previous office action, the examiner is including them in this rejection for the sake of clarity. It is believed this is not a new grounds of rejection, as claims 23 – 24 and 28 – 29 were all included in the rejection under 35 USC 102(a) as anticipated by Ruben, both in the previous office action and in the instant office action.

Applicant argues, on p. 6 of the remarks, that Ruben is not available as a reference under 35 USC 102(a) and thus cannot serve as a reference under 35 USC § 103. Applicant's arguments have been fully considered but they are not persuasive. For the reasons explained in detail in paragraph 4 above, declaration and provisional application are not sufficient to antedate the reference by Ruben. Therefore the rejection stands.

The examiner notes that applicant did not traverse the examiner's determination that it would have been obvious to one of ordinary skill in the art to label antibodies, as taught by Holmes.

7. Claims 22 – 26 and 28 – 30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ruben (US Patent Application Publication 2003/0100051) in view of Holmes (Current Protocols in Immunology, cited in previous office action).

As a preliminary matter, claims 23 – 24 and 28 – 29 are included in this rejection. While they were not explicitly listed in the grounds of rejection in the previous office action, the examiner is including them in this rejection for the sake of clarity. It is believed this is not a new grounds of rejection, as claims 23 – 24 and 28 – 29 were all included in the rejection under 35 USC 102(a) as anticipated by Ruben, both in the previous office action and in the instant office action.

Applicant argues, on pp. 10 – 11 of the remarks, that Ruben II is not available as a reference under 35 USC 102(e) and thus cannot serve as a reference under 35 USC § 103. Applicant's arguments have been fully considered but they are not persuasive. For the reasons

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explained in detail in paragraph 5 above, declaration and provisional application are not sufficient to antedate the reference by Ruben. Therefore the rejection stands.

The examiner notes that applicant did not traverse the examiner's determination that it would have been obvious to one of ordinary skill in the art to label antibodies, as taught by Holmes.

Conclusion

8. No claim is allowed.

9. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Daniel Kolker whose telephone number is (571) 272-3181. The examiner can normally be reached on Mon - Fri 8:30AM - 5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet Andres can be reached on (571) 272-0867. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.



Daniel E. Kolker, Ph.D.

August 14, 2006



ROBERT C. HAYES, PH.D.
PRIMARY EXAMINER

Appl. No. : 10/036,063
Filed : December 26, 2001

DELETION OF INVENTORS

Please correct the inventorship under 37 CFR §1.48(b) by removing the following inventors from the present application:

Luc Desnoyers, Dan L. Eaton, Timothy L. Stewart and Zemin Zhang.

DK
OK to enter
8/14/06